PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
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DUE ON AUG 14 2005
Reply to: PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(date/month/year)* 28 February 2005 (28-02-2005)

Applicant's or agent's file reference
6013-140PCT

FOR FURTHER ACTION
See paragraph 2 below

International application no
PCT/CA2004/001823

International filing date *(date/month/year)*
14 October 2004 (14-10-2004)

Priority date *(date/month/year)*
14 October 2003 (14-10-2003)

International Patent Classification (IPC) or both national classification and IP
IPC[7]: C07K-14/47, A01N-1/02, A61K-38/17, A61K-35-52

Applicant UNIVERSITE LAVAL ET AL

1. This opinion contains indications relating to the following items :

[X]	Box No. I	Basis of the opinion
[X]	Box No. II	Priority
[X]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[X]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[ ]	Box No. VI	Certain documents cited
[X]	Box No. VII	Certain defects in the international application
[X]	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**
If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA
Commissioner of Patents
Canadian Patent Office
Box PCT, Ottawa/Gatineau K1A 0C9

Facsimile No. (819) 953-9538

Authorized officer
Colleen MacFarlane (819) 997-4614

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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language which it was filed, unless otherwise indicated under this item.

[ ] This opinion has been established on the basis of a translation from the original language into the following language __ , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :

a. type of material

[ ] a sequence listing

[ ] table(s) related to the sequence listing

b. format of material

[ ] in written format

[ ] in computer readable from

c. time of filing/furnishing

[ ] contained in the international application as filed.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority for the purposes of search.

3. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments :

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Box No. II Priority

1 [] The following document has not yet been furnished :

[] copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

[ ] translation of the earlier application whose priority has been claimed (rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2 [ ] This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purpose of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary :

The ISA does not have in its possession a copy of the earlier application. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of :

[ ] the entire international application

[X] claims Nos. 1, 2, 5, 6, 11, 13, 14 and 16

because

[ ] the said international application, or the said claims Nos. ____ relate to the following subject matter which does not require an international preliminary examination *(specify)* :

[X] the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1, 2, 5, 6, 11, 13, 14 and 16 are so unclear that no meaningful opinion could be formed *(specify)* :

see Supplemental Box

[X] the claims, or said claims Nos: 1, 2, 5, 6, 11, 13, 14 and 16 are so inadequately supported by the description that no meaningful opinion could be formed.

[ ] no international search report has been established for said claims Nos

[ ] the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that :

the written form
- [ ] has not been furnished
- [ ] does not comply with the standard

the computer readable form
- [ ] has not been furnished
- [ ] does not comply with the standard

[ ] the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

[X] See Supplemental Box for further details.

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Box No. IV Lack of unity of invention

1 [ ] In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has :

[ ] paid additional fees

[ ] paid additional fees under protest

[ ] not paid additional fees

2 [ ] This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3 This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

[X] complied with

[ ] not complied with for the following reasons :

4 Consequently, this opinion has been established in respect of the following parts of the international application :

[X] all parts

[ ] the parts relating to claims Nos. ____

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Box No. V reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	3, 4, 9, 10, 12	YES
	Claims	1, 2, 7, 8, 11, 13-16	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1-4, 7-16	NO
Industrial applicability (IA)	Claims	1-4, 7-16	YES
	Claims	NONE	NO

2. Citations and explanations :

Reference is made to the following documents:

D1: ASQUITH et al. "Tyrosine phosphorylation activates surface chaperones facilitating sperm-zona recognition." Journal of Cell Science. July 15 2004, vol. 117(6), pages 3645-3657.

D2: ASQUITH et al. "Localisation and significance of molecular chaperones, heat shock protein 1(Hspd1) and tumor rejection antigen gp96 (Tra1), in the male reproductive tract and during capacitation and acrosome reaction." BOR Papers in Press [online], September 29, 2004, Accession No. DOI:10.1095/biolreprod.104.032270.

D3: ECROYD, et al. "Tyrosine phosphorylation of HSP-90 during mammalian sperm capacitation." Biology of Reproduction, December 2003, vol. 69, pages 1801-1807. (Published online before print July 30, 2003, Accession No. DOI 10.1095/biolreprod.103.017350)

D4: HUANG et al. "The decline of porcine sperm motility by geldanamycin, a specific inhibitor of heat-shock protein 90 (HSP90)." Theriogenology, 2000, vol. 53, pages 1177-1184.

D5: HUANG et al. "Substantial decrease of heat-shock protein 90 precedes the decline of sperm motility during cooling of boar spermatozoa." Theriogenology, 1999, vol. 51, pages 1007-1016.

D6: IKAWA et al. "Calmegin is required for fertilin α/β heterodimerization and sperm fertility." Developmental Biology, 2001, vol. 240, pages 254-261.

D7: IKAWA et al. "The putative chaperone calmegin is required for sperm fertility." Nature, June 1997, vol. 387, pages 607-611.

D8: OKABE et al. "The putative chaperone calmegin and sperm fertility." from "The Male Gamete" in Basic Science to Clinical Applications, pages 47-54. Editor: Claude Gagnon. Publisher: Cache River Press, Vienna, Ill., 1999.

In the event that the claimed priority date is not valid, documents D1 and D2 will become relevant.

1. NOVELTY

The problem to be solved in the instant application is the provision of polypeptides capable of binding chaperone receptors for preserving, restoring or improving the physiological properties of sperm cells in order to facilitate fertilization.

Document D3 discloses the tyrosine phosphorylation and activation of a HSP90 polypeptide during capacitation and implicates it, as a representative chaperone polypeptide, in the process by which sperm gain the ability to fertilize the oocyte. Accordingly, then, D3 anticipates claims 1, 2, 7, 8, 11 and 13-16 contravening Article 33(2) PCT.

Huang et al. report the decline in porcine sperm motility with exposure to geldanamycin, a specific HSP90 inhibitor, in D4 and that a substantial decrease in HSP90 precedes the decline of sperm motility in cooled boar spermatozoa in D5, implicating HSP90 as crucial to sperm motility. Claim 1, 2, 7, 8, 11 and 13-16 are therefore considered to be anticipated by D4 or D5 under Article 33(2) PCT.

Continued in Supplemental Box

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted :

There is no description of Figures 13 and 14 in the "Brief Description of Drawings" section in the description as is required under Rule 5.1(iv) PCT.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

The expressions, "a polypeptide capable of binding a chaperone receptor" (Claims 1, 11, 13 and 16) and "a molecule capable of binding sperm cell chaperone" (Claim 2), are functional definitions and do not clearly define the chemical structures and thus are not in compliance with Article 6 (PCT). Similarly, the terms, "matrix protein" (Claims 2, 5 and 14) and "analogs or fragments thereof" (Claims 2 and 14), are not clearly defined in terms of their specific chemical structures, also contravening Article 6 (PCT). In addition, these expressions and terms are so broad as to encompass compounds not contemplated by the Applicant and do not find adequate support in the description and are thus not in compliance with Article 5 (PCT).

The expression, "at least one" (Claim 2), is indefinite and does not comply with Article 6 (PCT) since it is unclear whether the claim encompasses a mixture/composition of polypeptides or whether the claim encompasses a singular polypeptide as suggested by parent claim 1.

Similarly, Claims 9 and 10 do not comply with Article 6 (PCT) as it is unclear as to whether these claims encompass compositions of a polypeptide in a "diluent medium" or whether the claims encompass the polypeptide itself as suggested by parent claim 1.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of Box III

The expressions, "a polypeptide capable of binding a chaperone receptor" (Claims 1, 11, 13 and 16) and "a molecule capable of binding sperm cell chaperone" (Claim 2), are functional definitions and do not clearly define the chemical structures and thus are not in compliance with Article 6 (PCT). Similarly, the terms, "matrix protein"(Claims 2, 5 and 14) and "analogs or fragments thereof" (Claims 2 and 14), are not clearly defined in terms of their specific chemical structures, also contravening Article 6 (PCT). In addition, these expressions and terms are so broad as to encompass compounds not contemplated by the Applicant and which do not find adequate support in the description and are thus not in compliance with Article 5 (PCT). Consequently, no opinion has been rendered for claims 1, 2, 5, 6, 11, 13, 14 and 16 insofar as they relate to said terms and expressions.

Continuation of Box V

Documents D6, D7 and D8 disclose the chaperone, calmegin, in relation to sperm fertility. With their disclosure in D7 that loss of endoplasmic reticulum calmegin results in the production of sterile sperm which do not bind to the zona pellicuda in calmegin -/- mice, Ikawa et al. further disclose in D6 that calmegin -/- sperm were defective in their migration into the oviduct and in adhesion to the egg plasma membrane. Taken together, D6 and D7 clearly demonstrate calmegin is required for sperm migration, zona pellucida adhesion and egg plasma membrane adhesion. D8 also discloses calmegin's crucial role in male fertility. Accordingly, documents D6, D7 and D8 are considered as novelty-destroying for claims 1, 2, 7, 8, 11 and 13-16 (Article 33(2)).

D3-D8 do not specifically disclose GRP 78, Sec A, Sec B, Sec Y and GroEL in relation to the physiological properties of sperm, nor do they disclose specific concentrations, compositions or methods using the chaperone polypeptides to improve the physiological properties of sperm. Claims 3, 4, 9, 10 and 12 are therefore considered novel under Article 33(2) PCT.

2. INVENTIVE STEP

Although the prior art does not specifically disclose a role for GRP 78 (Claim 4) or Sec A, Sec B, Sec Y or GroEL (Claim 2) or HSP60 (Claim 3) in male fertility, because of their structural and functional similarities to the other chaperone polypeptides discussed in D3-D8, particularly the heat shock proteins, it would be within the competence of a skilled technician to conclude that they would have a similar effect on sperm physiological properties. Similarly, an inventive step is not required to simply determine effective concentrations of the chaperone polypeptides (Claims 9, 10) or basic compositions comprising the chaperones (Claims 12). Thus, an inventive step cannot be acknowledged under Article 33(3) PCT for the subject matter of claims 3, 4, 9, 10 or 12 in view of D3-D8.

3. INDUSTRIAL APPLICABILITY

Claims 1-4 and 7-16 appear to define subject matter that has industrial applicability under Article 33(4) PCT based on the putative ability of chaperone polypeptides to improve physiological properties of sperm to facilitate fertilization.